EAST Search History (INCLUDING INTERFERENCE)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	5038	544/238 OR 544/295 OR 544/357 OR 514/252.02 OR 514/252.12 OR 514/255.05	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/10/11 07:40
L2	101	L1 AND (SODIUM ADJ CHANNEL)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/10/11 07:40
L3	32	L2 AND (AMILORIDE OR PYRAZINOYLGUANIDINE OR (PYRAZINYL ADJ GUANIDINE) OR (GUANIDINOYL ADJ PYRAZINE))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/10/11 07:41

10/828,329

STN SEARCH TRANSCRIPT

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 4	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 5	MAY 11	KOREAPAT updates resume
NEWS 6	MAY 19	Derwent World Patents Index to be reloaded and enhanced
NEWS 7	MAY 30	IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS 8	MAY 30	The F-Term thesaurus is now available in CA/CAplus
NEWS 9	JUN 02	The first reclassification of IPC codes now complete in INPADOC
NEWS 10	JUN 26	TULSA/TULSA2 reloaded and enhanced with new search and and display fields
NEWS 11	JUN 28	Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 12	JUl 11	CHEMSAFE reloaded and enhanced
NEWS 13	JUl 14	FSTA enhanced with Japanese patents
NEWS 14	JUl 19	Coverage of Research Disclosure reinstated in DWPI
NEWS 15	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 16	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 17	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 18	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 19	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 20	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 21	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 22	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 23	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme

NEWS EXPRESS	JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:38:06 ON 11 OCT 2006

=> FILE REG

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 08:38:19 ON 11 OCT 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 OCT 2006 HIGHEST RN 910095-75-9
DICTIONARY FILE UPDATES: 10 OCT 2006 HIGHEST RN 910095-75-9

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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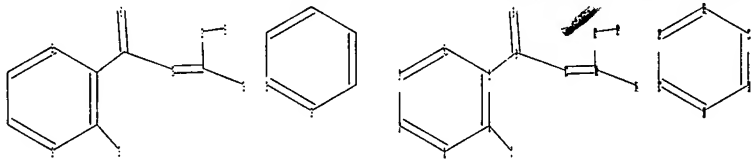

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7 8 9 10 11 12 13 14
ring nodes :
1 2 3 4 5 6 16 17 18 19 20 21
chain bonds :
5-8 6-7 8-9 8-10 10-11 11-12 11-14 12-13
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-21 17-18 18-19 19-20 20-21
exact/norm bonds :
6-7 8-9 8-10 10-11 11-12 11-14
exact bonds :
5-8 12-13
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-21 17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom

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L1 HAS NO ANSWERS
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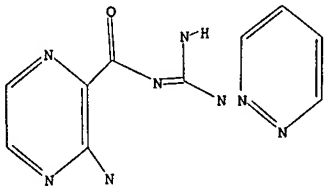

"G" RING IS
1,2 - DIAZINE

Structure attributes must be viewed using STN Express query preparation.

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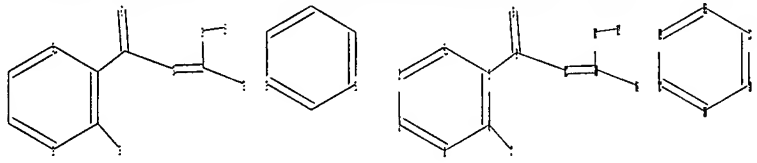

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7 8 9 10 11 12 13 14
ring nodes :
1 2 3 4 5 6 16 17 18 19 20 21
chain bonds :
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ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-21 17-18 18-19 19-20 20-21
exact/norm bonds :
6-7 8-9 8-10 10-11 11-12 11-14
exact bonds :
5-8 12-13
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-21 17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
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L2 STRUCTURE UPLOADED

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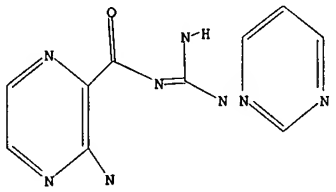
L2 HAS NO ANSWERS
L2 STR



"Q" RING IS
1,3 - DIAZINE

Structure attributes must be viewed using STN Express query preparation.

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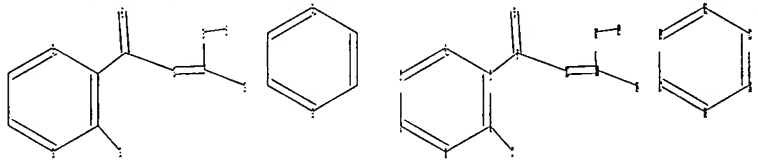

chain nodes :
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ring nodes :
1 2 3 4 5 6 16 17 18 19 20 21
chain bonds :
5-8 6-7 8-9 8-10 10-11 11-12 11-14 12-13
ring bonds :
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exact/norm bonds :
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exact bonds :
5-8 12-13
normalized bonds :
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isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 16:Atom 17:Atom 18:Atom 19:Atom
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L3 STRUCTURE UPLOADED

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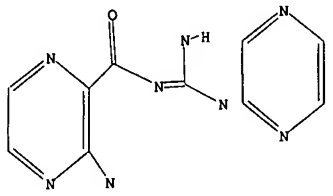
L3 HAS NO ANSWERS

L3 STR



"Q" RING IS 1,4 - DIAZINE

SEARCHED ALL THREE

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -        0 TO ITERATE

100.0% PROCESSED         0 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:   ONLINE  **COMPLETE**
                         BATCH   **COMPLETE**
PROJECTED ITERATIONS:             0 TO        0
PROJECTED ANSWERS:                0 TO        0

L4            0 SEA SSS SAM L1

=> S L2
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SAMPLE SCREEN SEARCH COMPLETED -        3 TO ITERATE

100.0% PROCESSED         3 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:   ONLINE  **COMPLETE**
                         BATCH   **COMPLETE**
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PROJECTED ANSWERS:                0 TO        0

L5            0 SEA SSS SAM L2

=> S L3
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SEARCH TIME: 00.00.01

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                         BATCH   **COMPLETE**
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PROJECTED ANSWERS:                2 TO      124

L6            2 SEA SSS SAM L3

=> S L1 SSS FULL
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100.0% PROCESSED        12 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

L7             0 SEA SSS FUL L1

=> S L2 SSS FULL
FULL SEARCH INITIATED 08:39:57 FILE 'REGISTRY'
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100.0% PROCESSED        71 ITERATIONS                             18 ANSWERS
SEARCH TIME: 00.00.01

L8            18 SEA SSS FUL L2

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100.0% PROCESSED        71 ITERATIONS                             20 ANSWERS
SEARCH TIME: 00.00.01

L9            20 SEA SSS FUL L3

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COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                              ENTRY    SESSION
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=> S L8 OR L9
             7 L8
             4 L9
L10         11 L8 OR L9

=> D 1-11 IBIB ABS HITSTR

L10  ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2005:346797  CAPLUS
DOCUMENT NUMBER:         142:411366
TITLE:                   Preparation of pyridazinylcarbonyl-substituted ureas
                         used for reducing risk of infection from pathogens
INVENTOR(S):             Johnson, Michael R.; Hopkins, Samuel E.
```

PATENT ASSIGNEE(S): Parion Sciences, Inc., USA
SOURCE: PCT Int. Appl., 218 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005034847	A2	20050421	WO 2004-US26963	20040819
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005090505	A1	20050428	US 2004-920626	20040818
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EP 1656096	A2	20060517	EP 2004-809587	20040819
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US 2006205738	A1	20060914	US 2005-211707	20050826

PRIORITY APPLN. INFO.:			
US 2003-496481P	P	20030820
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US 2003-495720P	P	20030818
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US 2004-920410	A3	20040818
WO 2004-US26963	W	20040819

OTHER SOURCE(S): MARPAT 142:411366
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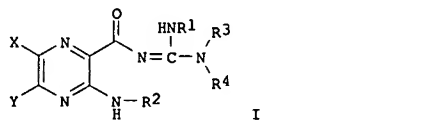

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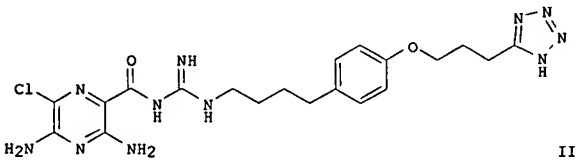


II

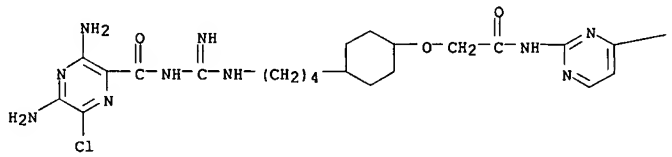
AB Title compds. I [X = H, halo, CF3, etc.; Y = H, OH, SH, etc.; R1 = H, alkyl; R2 = alkoxy, etc.; R3-4 = H, alkyl, OH, alkyl, Ph, etc.] are prepared

For instance, II is prepared in 4 steps from [4-(4-hydroxyphenyl)butyl]carbamic acid benzyl ester (preparation given), 4-bromobutyronitrile and 1-(3,5-diamino-6-chloropyrazine-2-carbonyl)-2-methylisothiourea•HI. II has EC50 = 25 nM in a sodium channel blocker assay. I are useful for prophylactic treatment to one or more members of a population at risk of exposure to or already exposed to one or more airborne pathogens, either from natural sources or from intentional release of pathogens into the environment.

IT *845753-79-9P 847200-87-7P 847200-90-2P*
847200-91-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridazinylcarbonyl-substituted ureas used for reducing risk of infection from pathogens)

RN 845753-79-9 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(4-amino-2-pyrimidinyl)amino]-2-oxoethoxy]cyclohexyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

PAGE 1-A

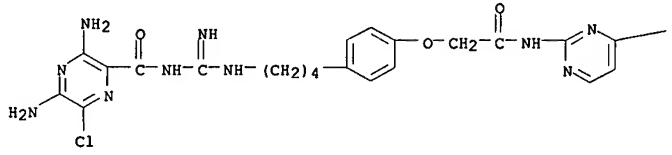


PAGE 1-B

—NH2

RN 847200-87-7 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(4-amino-2-pyrimidinyl)amino]-2-oxoethoxy]phenyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

—NH2

RN 847200-90-2 CAPLUS
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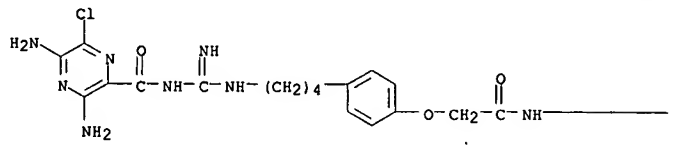
PAGE 1-A



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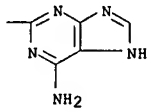

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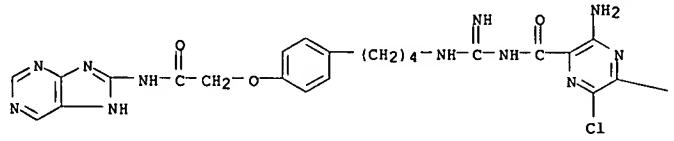
PAGE 1-A



PAGE 1-B

L10 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:177896 CAPLUS
DOCUMENT NUMBER: 142:280225
TITLE: Preparation of capped aminopyrazinoylguanidines as sodium channel blockers

INVENTOR(S): Johnson, Michael R.; Molino, Bruce F.; Zhang, Jianzhong; Sargent, Bruce J.
PATENT ASSIGNEE(S): Parion Sciences, Inc., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018644	A1	20050303	WO 2004-US26885	20040818
WO 2005018644	B1	20050512		
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OTHER SOURCE(S): MARPAT 142:280225
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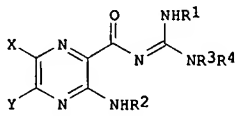


I

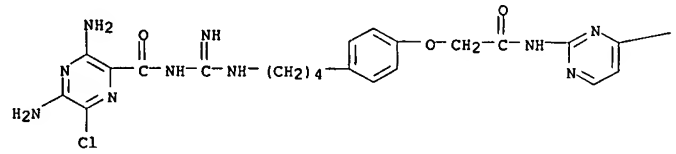
AB Title compds. [I; X = H, halo, CF3, alkyl, (substituted) Ph, etc.; Y = H, OH, SH, alkoxy, alkylthio, halo, alkyl, (substituted) aryl, etc.; R1 = H, alkyl; R2 = R7, (CH2)mOR8, (CH2)mNR7R10, (CH2CH2O)mR8, etc.; m = 1-7; R3, R4 = H, alkyl, hydroxyalkyl, Ph, phenylalkyl, naphthylalkyl, pyridylalkyl, etc.; R7 = H, alkyl, (substituted) Ph, etc.; R8 = H, alkyl, 2-tetrahydropyranyl, glucuronide, etc.; R10 = H, SO2Me, COR13, CO2R13, etc.; R13 = H, R7, R10, etc.; with provisos], were prepared Thus, [4-(4-hydroxyphenyl)butyl]carbamic acid benzyl ester in EtOH at 70° was treated with oxiranylmethanol over 4 h to give 4.6% [4-[4-[3-(2,3-dihydroxypropoxy)-2-hydroxypropoxy]phenyl]butyl]carbamic acid benzyl ester. This was hydrogenolyzed in EtOH over Pd/C to give 51% 3-[3-[4-(4-aminobutyl)phenoxy]-2-hydroxypropoxy]propane-1,2-diol. The

latter was stirred with Et3N and 1-(3,5-diamino-6-chloropyrazine-2-carbonyl)-2-methylisothiourea hydroiodide in EtOH at 65° to give 36% N-(3,5-diamino-6-chloropyrazine-2-carbonyl)-N'-[4-[4-[3-(2,3-dihydroxypropoxy)-2-hydroxypropoxy]phenyl]butyl]guanidine (PSA 15143). The latter showed Na channel blocking activity with EC50 = 7 nM.

IT *847200-87-7P 847200-90-2P 847200-91-3P*
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of aminopyrazinoylguanidines as sodium channel blockers)

RN 847200-87-7 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(4-amino-2-pyrimidinyl)amino]-2-oxoethoxy]phenyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

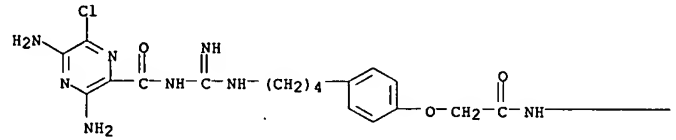
PAGE 1-A



PAGE 1-B

RN 847200-90-2 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(6-amino-1H-purin-2-yl)amino]-2-oxoethoxy]phenyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

PAGE 1-A



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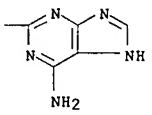
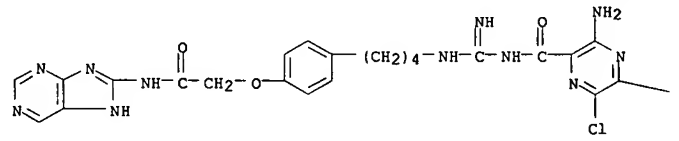


RN 847200-91-3 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[imino[[4-[4-[2-oxo-2-(1H-purin-8-ylamino)ethoxy]phenyl]butyl]amino]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:158635 CAPLUS
DOCUMENT NUMBER: 142:261557
TITLE: Preparation of cyclic pyrazinoylguanidine sodium channel blockers
INVENTOR(S): Johnson, Michael R.
PATENT ASSIGNEE(S): Parion Sciences, Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

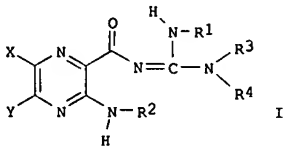
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016879	A2	20050224	WO 2004-US26880	20040818
WO 2005016879	A3	20050602		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

AU 2004264441	A1	20050224	AU 2004-264441		20040818
CA 2534569	AA	20050224	CA 2004-2534569		20040818
US 2005059676	A1	20050317	US 2004-920353		20040818
EP 1670474	A2	20060621	EP 2004-801870		20040818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
US 2006205738	A1	20060914	US 2005-211707		20050826
PRIORITY APPLN. INFO.:			US 2003-495720P	P	20030818
			US 2004-920410	A3	20040818
			WO 2004-US26880	W	20040818

OTHER SOURCE(S): CASREACT 142:261557; MARPAT 142:261557
GI



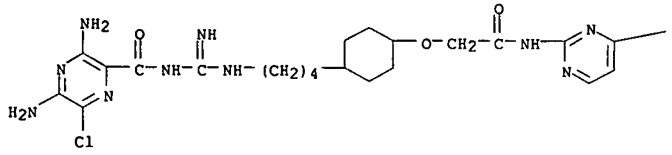
I

AB The title compds. I [X = halo, etc.; Y = H, hydroxyl, etc.; R1 = H, alkyl; R2 = R7, etc.; R3, R4 = H, alkyl, etc.; R7 = (un)substituted Ph, etc], useful as sodium channel blockers (no data), are prepared Thus, N-(3,5-diamino-6-chloropyrazine-2-carbonyl)-N'-[4-[1-(2-hydroxyethyl)piperidin-4-yl]butyl]guanidine dihydrochloride was prepared in a multistep process starting from 4-(piperidin-4-yl)butyric acid HCl salt.

IT *845753-79-9P*
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic pyrazinoylguanidine sodium channel blockers)

RN 845753-79-9 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(4-amino-2-pyrimidinyl)amino]-2-oxoethoxy]cyclohexyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

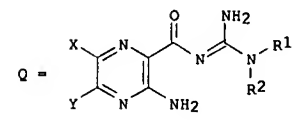


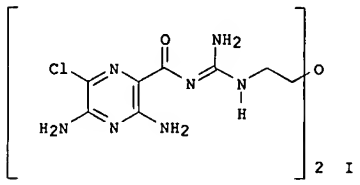
L10 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:63982 CAPLUS
DOCUMENT NUMBER: 134:115971
TITLE: Pyrazinoylguanidine derivatives as conjugates of sodium channel blockers and methods of using the same for hydrating mucosal surfaces
INVENTOR(S): Boucher, Richard C., Jr.
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

THIS IS PRIOR ART

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001005773	A1	20010125	WO 2000-US19775		20000719
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2378181	AA	20010125	CA 2000-2378181		20000719
EP 1196396	A1	20020417	EP 2000-948820		20000719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
US 6475509	B1	20021105	US 2000-618978		20000719
NZ 516595	A	20030725	NZ 2000-516595		20000719
JP 2004513870	T2	20040513	JP 2001-511434		20000719
AU 774865	B2	20040708	AU 2000-62262		20000719
ZA 2002000129	A	20030407	ZA 2002-129		20020107
NO 2002000242	A	20020319	NO 2002-242		20020116
US 2002165239	A1	20021107	US 2002-121913		20020412
US 6607741	B2	20030819			
US 2002158255	A1	20030902	US 2002-121917		20020412
US 6613345	B2	20030902			
PRIORITY APPLN. INFO.:			US 1999-144479P	P	19990719
			US 2000-618978	A	20000719
			WO 2000-US19775	W	20000719

OTHER SOURCE(S): MARPAT 134:115971
GI

Q = 



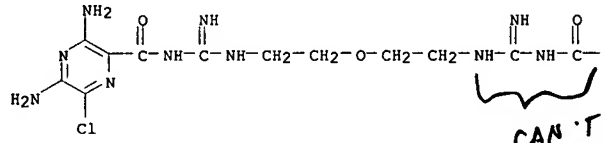
AB Compds. of the general formula P1-L-P2 [L = linker; P1 = a pyrazinoylguanidine sodium channel blocker; P2 = a dinucleotide, a pyrazinoylguanidine sodium channel blocker and/or a P2Y2 receptor agonist; P1 and P2 may be independently Q wherein X = halo, alkyl, cycloalkyl, (un)substituted Ph, alkylthio, alkylsulfonyl, oxyalkylthio, oxyalkylsulfonyl, phenylalkylthio and phenylalkylsulfonyl; Y = OH, mercapto, alkyloxy, alkylthio, Cl, alkyl, cycloalkyl, Ph and amino derivs.; R1 and R2 are independently selected from H, alkyl, hydroxyalkyl, (un)substituted phenylalkyl, etc.; L = alkyl, hydroxyalkyl, (un)substituted arylalkyl, etc.] are prepared and disclosed as conjugates of sodium channel blockers. Thus, I was prepared via substitution reactions of N-Cbz-1-(3,5-diamino-6-chloropyrazinoyl)-2-methylpseudothiourea with 1,5-diamino-3-oxapentane. I possessed an IC50 value of 1275 nM in an assay for Na+ channel subunit expression in Xenopus oocytes, and was found to absorb into cells less rapidly than amiloride. Pharmaceutical formulations containing the disclosed compds. and methods of use thereof to hydrate mucosal surfaces such as airway mucosal surfaces are also disclosed.

IT *321554-65-8P 321554-67-0P 321554-68-1P*
321554-69-2P 321554-70-5P 321554-71-6P
321554-72-7P 321554-73-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazinoylguanidine derivs. as conjugates of sodium channel blockers used for hydration of mucosal surfaces)

RN 321554-65-8 CAPLUS
CN Pyrazinecarboxamide, N,N'-[oxybis(2,1-ethanediyliminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)

BIS-AMILORIDE COMPDS:

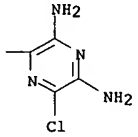
PAGE 1-A



CAN'T BE IN (A) LINKER

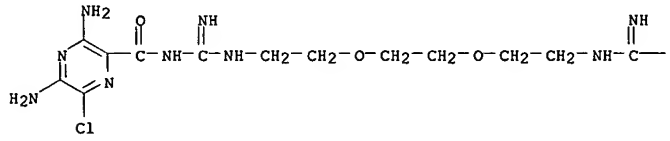
●2 HBr

PAGE 1-B



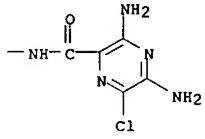
RN 321554-67-0 CAPLUS
CN Pyrazinecarboxamide, N,N'-(1,12-diimino-5,8-dioxa-2,11-diazadodecane-1,12-diyl)bis[3,5-diamino-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

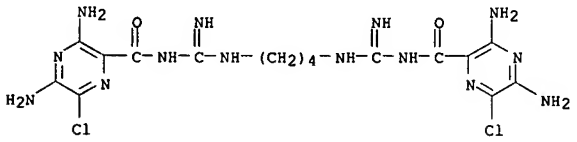


●2 HCl

PAGE 1-B



RN 321554-68-1 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,4-butanediylbis(iminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

RN 321554-69-2 CAPLUS
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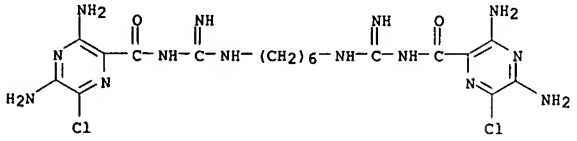
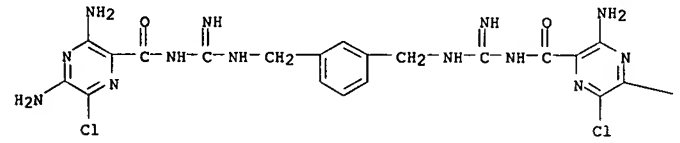


●2 HBr

RN 321554-70-5 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,3-phenylenebis(methyleneiminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)

PAGE 1-A



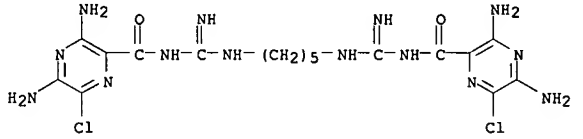
●2 HBr

PAGE 1-B

NH2

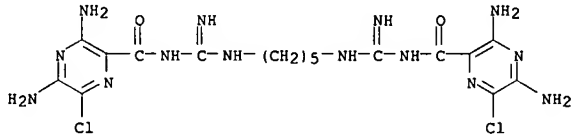
RN 321554-71-6 CAPLUS

CN Pyrazinecarboxamide, N,N'-[1,5-pentanediylbis(iminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

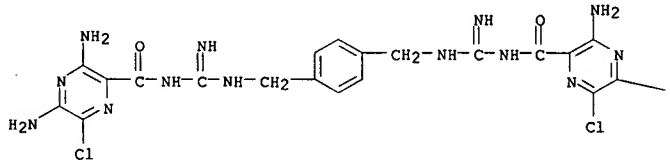
RN 321554-72-7 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,5-pentanediylbis(iminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

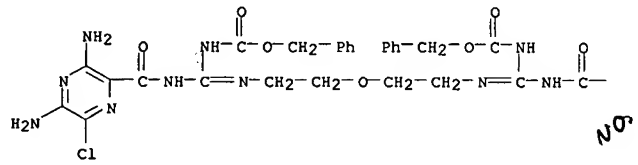
RN 321554-73-8 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,4-phenylenebis(methyleneiminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)

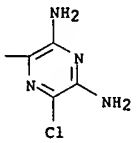
PAGE 1-A



●2 HBr

IT *321554-75-0P*
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrazinoylguanidine derivs. as conjugates of sodium channel blockers used for hydration of mucosal surfaces)
RN 321554-75-0 CAPLUS
CN 7-Oxa-2,4,10,12-tetraazatrideca-2,10-dienedioic acid, 3,11-bis[[(3,5-diamino-6-chloropyrazinyl)carbonyl]amino]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)





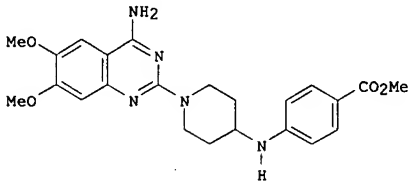
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:855763 CAPLUS
DOCUMENT NUMBER: 134:29423
TITLE: Preparation of [(quinazolinylpiperidinyl)amino]benzoates and analogs as bactericides
INVENTOR(S): Kung, Pei-Pei; Cook, Phillip Dan; Guinosso, Charles John
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: U.S., 22 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6156758	A	20001205	US 1999-391843	19990908
PRIORITY APPLN. INFO.:			US 1999-391843	19990908
OTHER SOURCE(S):	MARPAT 134:29423			

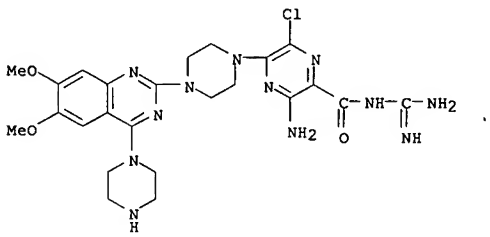
GI



II

AB RZ(NR4)nZCO2R1 [I; R = (un)substituted 2-quinazolinyl; R1 = OH, (ar)alkoxy, aryloxy, etc.; R4 = H, alkyl, acyl; Z = piperidine- or piperazine-1,4-diyl; Z1 = (un)substituted 1,4-phenylene, -pyridine-2,5- or -5,2-diyl, -pyrazine-2,5-diyl; n = 0 or 1] were prepared Thus, Me 3-amino-5,6-dichloro-2-pyrazinecarboxylate was condensed with 1-protected-4-aminopiperidine and the deprotected product condensed with 4-amino-2-chloro-6,7-dimethoxyquinazoline to give title compound II. Data for biol. activity of I were given.

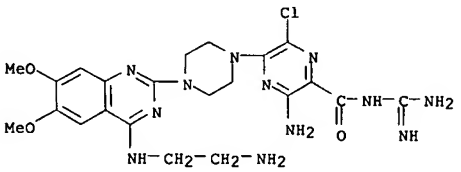
IT *310901-30-5P 310901-33-8P*
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of [(quinazolinylpiperidinyl)amino]benzoates and analogs as bactericides)
RN 310901-30-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[6,7-dimethoxy-4-(1-piperazinyl)-2-quinazolinyl]-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 310901-33-8 CAPLUS

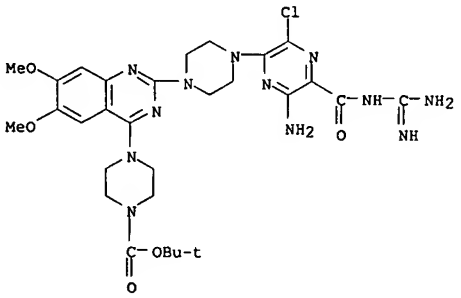
CN Pyrazinecarboxamide, 3-amino-5-[4-[4-[(2-aminoethyl)amino]-6,7-dimethoxy-2-quinazolinyl]-1-piperazinyl]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



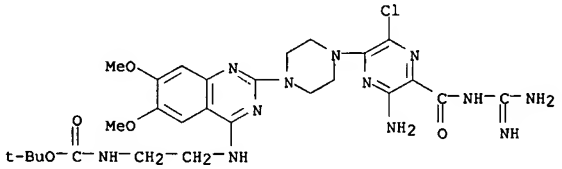
●2 HCl

IT *310901-41-8P 310901-46-3P*
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [(quinazolinylpiperidinyl)amino]benzoates and analogs as bactericides)

RN 310901-41-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[2-[4-[6-amino-5-[[(aminoiminomethyl)amino]carbonyl]-3-chloropyrazinyl]-1-piperazinyl]-6,7-dimethoxy-4-quinazolinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 310901-46-3 CAPLUS
CN Carbamic acid, [2-[[2-[4-[6-amino-5-[[(aminoiminomethyl)amino]carbonyl]-3-chloropyrazinyl]-1-piperazinyl]-6,7-dimethoxy-4-quinazolinyl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:789190 CAPLUS
DOCUMENT NUMBER: 123:198830
TITLE: Preparation of amidinocarbamoylpyrazines as drugs.
INVENTOR(S): Roos, Otto; Speck, Georg; Loesel, Walter; Arndts, Dietrich
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4337609	A1	19950511	DE 1993-4337609	19931104
CA 2175837	AA	19950511	CA 1994-2175837	19941031
WO 9512592	A1	19950511	WO 1994-EP3580	19941031
W: AM, AU, BG, CA, CN, CZ, FI, GE, HU, JP, KR, KZ, LT, LV, NO, NZ, PL, RO, RU, SI, SK, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9479936	A1	19950523	AU 1994-79936	19941031
AU 690588	B2	19980430		
EP 726899	A1	19960821	EP 1994-931018	19941031
EP 726899	B1	20000119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1134151	A	19961023	CN 1994-194016	19941031
JP 09505035	T2	19970520	JP 1994-513010	19941031
AT 188965	E	20000215	AT 1994-931018	19941031
ES 2140565	T3	20000301	ES 1994-931018	19941031
ZA 9408669	A	19950704	ZA 1994-8669	19941103
GR 3033034	T3	20000831	GR 2000-400720	20000322

PRIORITY APPLN. INFO.: DE 1993-4337609 A 19931104
WO 1994-EP3580 W 19941031

OTHER SOURCE(S): MARPAT 123:198830
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

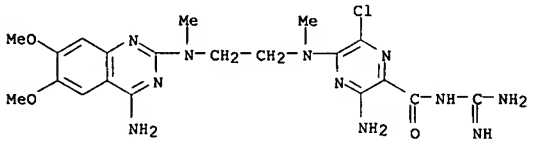
AB Title compds. [I; R1 = H, (hydroxy-substituted, O-interrupted) alkyl, alkenyl, alkynyl, Ph, cycloalkyl, etc.; R2 = Q1, Q2, etc.; R1R2N = Q3, etc.], were prepared as inhibitors of Na+/H+ and Na+/Li+ exchange useful as antihypertensives, antiischemics, mucolytics, diuretics, anticancer

agents, etc. (no data). Thus, N-(4-amino-6,7-dimethoxy-2-quinazolinyl)-N,N'-dimethyl-1,2-diaminoethane, Me 3-amino-5,6-dichloropyrazine-2-carboxylate, and Et3N were heated in Me2SO at 80° to give a residue which was stirred with guanidine hydrochloride in methanolic NaOMe to give Me 3-amino-6-chloro-5-[2-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-(N,N'-dimethyl-1,2-dimaminoethyl)]pyrazine-2-carboxylate. This was refluxed in DMF and the residue was treated with HCl in EtOH to give title compound (II).

IT *167684-27-7P*
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidinocarbamoylpyrazines as drugs)

RN 167684-27-7 CAPLUS

CN Pyrazinecarboxamide, 3-amino-5-[[2-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]ethyl]methylamino]-N-(aminoiminomethyl)-6-chloro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L10 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:449413 CAPLUS
DOCUMENT NUMBER: 119:49413
TITLE: New pyrazine derivatives, their preparation and their use as ingredients in drugs
INVENTOR(S): Koeppe, Herbert; Speck, Georg; Stockhaus, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim KG
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

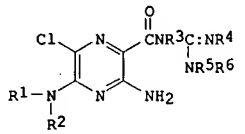
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9304048	A1	19930304	WO 1992-EP1738	19920731
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
DE 4127026	A1	19930218	DE 1991-4127026	19910816
DE 4130461	A1	19930318	DE 1991-4130461	19910913
AU 9223870	A1	19930316	AU 1992-23870	19920731
AU 669122	B2	19960530		
EP 598770	A1	19940601	EP 1992-916697	19920731
EP 598770	B1	19971015		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06509798	T2	19941102	JP 1992-504057	19920731
NO 9400523	A	19940215	NO 1994-523	19940215

PRIORITY APPLN. INFO.:

DE 1991-4127026	A	19910816
DE 1991-4130461	A	19910913
WO 1992-EP1738	A	19920731

OTHER SOURCE(S): CASREACT 119:49413; MARPAT 119:49413

GI



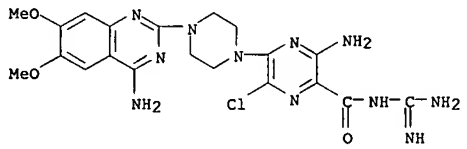
I

AB A process for the preparation of pyrazine derivative I where R1 = H or alkyl, R2 =
functionalized alkyl moiety, R3, R5 = H and R4, R6 = H, Me, Et, Bu, benzyl was accomplished by conventional methods. E.g., reaction of 4.44 g of Me 3-amino-5,6-dichloropyrazine-2-carboxylate and 3.6 g of 2-amino-1-(2,6-dimethylphenoxy)propane with 2.2 g Et3N in 40 mL anhydrous DMF gave an intermediate pyrazinecarboxylic acid ester which underwent subsequent ammonolysis in 50 mL MeOH and 80mL of methanolic guanidine solution and eluted on silica gel by AcOH:i-PrOH:NH3 eluent to give N-amidino-3-amino-6-chloro-5-(2-[1-(2,6-dimethylphenoxy)]propylamino)pyrazine-2-carboxamide-hydrochloride. The products are suitable for use as active ingredients in drugs (no data).

IT *147894-06-2P 147894-29-9P 147932-13-6P*
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 147894-06-2 CAPLUS

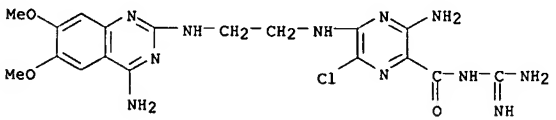
CN Pyrazinecarboxamide, 3-amino-5-[4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

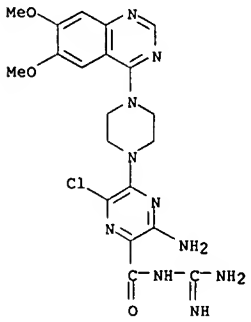
RN 147894-29-9 CAPLUS

CN Pyrazinecarboxamide, 3-amino-5-[[2-[(4-amino-6,7-dimethoxy-2-quinazolinyl)amino]ethyl]amino]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 147932-13-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(6,7-dimethoxy-4-quinazolinyl)-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

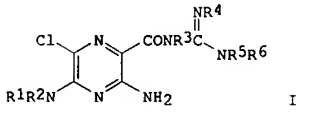
L10 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:408831 CAPLUS
DOCUMENT NUMBER: 119:8831
TITLE: Preparation of 2-guanidinocarbonyl-3,5-diamino-6-chloropyrazines as drugs
INVENTOR(S): Koeppe, Herbert; Speck, Georg; Stockhaus, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4127026	A1	19930218	DE 1991-4127026	19910816
WO 9304048	A1	19930304	WO 1992-EP1738	19920731

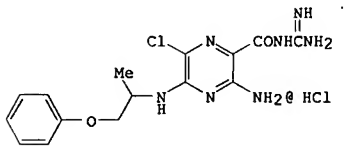
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

AU 9223870	A1	19930316	AU 1992-23870	19920731
AU 669122	B2	19960530		
EP 598770	A1	19940601	EP 1992-916697	19920731
EP 598770	B1	19971015		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06509798	T2	19941102	JP 1992-504057	19920731
HU 67661	A2	19950428	HU 1994-430	19920731
CZ 280760	B6	19960417	CZ 1994-337	19920731
AT 159250	E	19971115	AT 1992-916697	19920731
ES 2108129	T3	19971216	ES 1992-916697	19920731
RU 2124008	C1	19981227	RU 1994-15265	19920731
ZA 9206132	A	19930331	ZA 1992-6132	19920814
NO 9400523	A	19940215	NO 1994-523	19940215
PRIORITY APPLN. INFO.:			DE 1991-4127026 A	19910816
			DE 1991-4130461 A	19910913
			WO 1992-EP1738 A	19920731

OTHER SOURCE(S): MARPAT 119:8831
GI

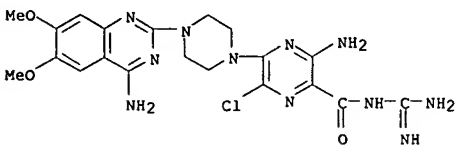


I



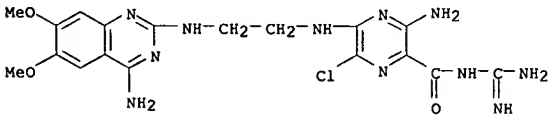
II

AB Title compds. [I; R1 = H, alkyl; R2 = morpholino, (substituted) alkyl, 4-piperidinyl, amidino; R1R2N = (substituted) piperidinyl, piperazinyl; R3-R6 = H, alkyl, PhCH2], effective inhibitors of Na+/H+ and Na+/Li+ exchange useful as antihypertensives, mucolytics, diuretics, neoplasm inhibitors, and platelet activating factor antagonists (no data), are prepared Thus, Me 3-amino-5,6-dichloropyrazine-2-carboxylate, 2-amino-1-(2,6-dimethylphenoxy)propane, and Et3N were heated in DMF at 95-100° for 1.5 h to give Me 3-amino-6-chloro-5-[2-[1-(2,6-dimethylphenoxy)]propylamino]pyrazine-2-carboxylate. This was heated with guanidine in MeOH to give title compound II.
IT *147894-06-2P 147894-29-9P 147932-13-6P*
147932-29-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)
RN 147894-06-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-[4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



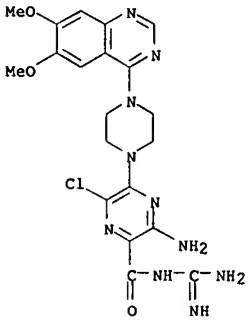
●2 HCl

RN 147894-29-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-[[2-[(4-amino-6,7-dimethoxy-2-quinazolinyl)amino]ethyl]amino]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



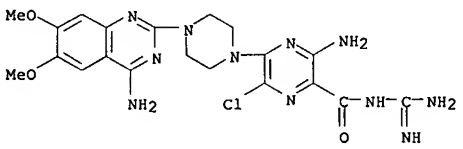
●2 HCl

RN 147932-13-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(6,7-dimethoxy-4-quinazolinyl)-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 147932-29-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-[4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl]-N-(aminoiminomethyl)-6-chloro- (9CI) (CA INDEX NAME)

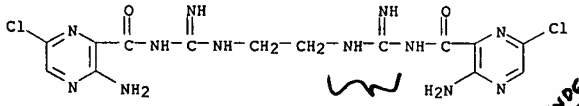


L10 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:37949 CAPLUS
DOCUMENT NUMBER: 66:37949
TITLE: Pyrazinoylguanidines
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: Neth. Appl., 17 pp.
CODEN: NAXXAN
DOCUMENT TYPE: Patent
LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6504569		19661010	NL 1965-4569	19650409
FR 1479232			FR	
FR 4498			FR	

OTHER SOURCE(S): MARPAT 66:37949
GI For diagram(s), see printed CA Issue.
AB The title compds. I (X = halogen; R1-4 = H or alkyl) are prepared by reaction of 3-(NRR-substituted)-6-(X-substituted)-pyrazine-2-carboxylic acid esters (II) with guanidines H2NC-(:NR2)NR3R4 (III). Thus, through 1.5 g. 3-(methylamino)-pyrazine-2-carboxylic acid in 250 ml. MeOH was passed HCl gas, the solution evaporated, neutralized with NaHCO3 solution, treated with 0.5 cc. Br, and filtered to obtain 1.7 g. Me ester of 3-(methylamino)-6-bromopyrazine-2-carboxylic acid (IV), m. 181.5-3.5°(iso-PrOH). Na (0.69 g.) was dissolved in 90 ml. MeOH; to the cold solution 3.01 g. dry powdered guanidine-HCl was added and the mixture refluxed 30 min. and filtered; to the filtrate 2 g. IV was added to give 1.1 g. [3-methylamino)-6-bromo-2-purazinoyl]-guanidine, m. 230.5-1.5°. To 23 g. Me ester of 3-amino-6-bromopyrazine-2-carboxylic acid in 40 cc. AcOH and 114 cc. 48% HBr at 5-10° a solution of 15 cc. Br in 40 cc. AcOH was added and the mixture treated at 0-5° with 17.4 g. NaNO2 in 30 cc. H2O in 1.5 hrs. To this stirred mixture at 20° 200 ml. 10N NaOH and saturated NaHSO3 solution was added to give 17.4 g. Me ester of 3,6-dibromopyrazine-2-carboxylic acid (V), m. 66-8° (aqueous EtOH). V (6 g.) and piperidine 30 min. at 25° gave the 3-piperidino derivative of V, m. 88-9°; its guanidino derivative m. 220-2°. Me2NH (15 g.) and 6 g. V gave the 3-Me2N derivative of V, m. 105-8°; its guanidino derivative m. 216-18°. The Me ester of 3-bromo-6-chloropyrazine-2-carboxylic acid, m. 35-6° gave the 3-[2-(dimethylamino)ethylamino] derivative, m. 105-8°; its guanidine derivative m. 221-13°. Ethylenebis[3-(3-amino-6-chloro-2-pyrazinoyl)guanidine]-2HCl, m. 323°. Treatment of β-amino-6-chloro-2-pyrazinoyl)guanidine with AcCl gave the 2,3-diacetylguanidine derivative, m. 187.5-8.5°; the analogous 2,3-di-Bz derivative m. 215-17°. [TABLE OMITTED] Other I (R = R1 = H) given in the table were prepared The compds. are diuretics.
IT *13301-07-0P*

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 13301-07-0 CAPLUS
CN Pyrazinecarboxamide, N,N'-[ethylenebis(iminoimidocarbonyl)]bis[3-amino-6-chloro-, dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

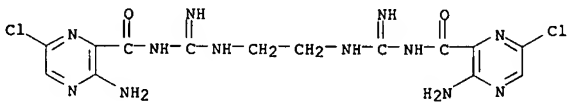
NOT IN CL 82 (THE INDEPENDENT CL.) GUANIDYL NOT PERMITTED IN (A) AS A LINKER

L10 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:10961 CAPLUS
DOCUMENT NUMBER: 66:10961
TITLE: Pyrazinoylguanidines
INVENTOR(S): Cragoe, Edward J., Jr.; Southwick, Philip L.
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: Belg., 25 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 662507		19651004		
GB 1095792			GB	
US 3240780		19660315	US 1963-332901	19631223
PRIORITY APPLN. INFO.:			US	19631223

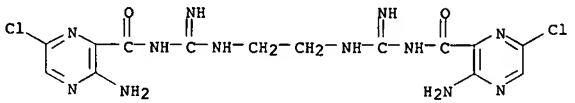
GI For diagram(s), see printed CA Issue.
AB Pyrazinoylguanidines (I) having diuretic and natriuretic properties are prepared Thus, 1.5 g. 3-methylaminopyrazinoic acid in 250 ml. MeOH is treated with gaseous HCl until saturation, the solution refluxed 2 hrs. and evaporated to dryness, saturated NaHCO3 aqueous solution added until pH 7 is reached, and 0.5 ml. Br added to give 1.7 g. Me 3-methylamino-6-bromopyrazinoate (III), m. 181.5-3.5° (iso-PrOH). Na (0.69 g.) is dissolved in 90 ml. MeOH, 3.02 g. guanidine hydrochloride added, the solution refluxed 30 min., precipitated NaCl filtered off, 2 g. III added, and the mixture heated for a short period and kept 1 hr. at room temperature to give 1.1 g. IV. The following compds. are similarly prepared (m.p. given): Me 3,6-dibromopyrazinoate, 66-8°; Me 3-piperidino-6-bromopyrazinoate, 88-90°; Me 3-dimethylamino-6-bromopyrazinoate, 80-2; Me 3-bromo-6-chloropyrazinoate, 35-6°; Me 3-(2-dimethylaminoethylamino)-6-chloropyrazinoate, 105-8°; ethylenebis[3-(3-amino-6-chloro-2-pyrazinoyl)guanidine],-(HCl salt m. 323°); 1-(3-amino-6-chloropyrazinoyl)-2,3-diacetylguanidine -; 1-(3-amino-6-chloropyrazinoyl)-2,3-dibenzoylguanidine, 215-17°; 1-(3-metnylamino-6-trifluoromethylpyrazinoyl)-3-benzylguanidine, -; 1-(3-amino-6-trifluoromethylpyrazinoyl)-2,3-diacetylguanidine, -; 1-(3-amino-6-trifluoromethylpyrazinoyl)-3,3-dimethylguanidine, -. Similarly prepared were the tabulated I. [TABLE OMITTED]
IT *13301-07-0P*

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 13301-07-0 CAPLUS
CN Pyrazinecarboxamide, N,N'-[ethylenebis(iminoimidocarbonyl)]bis[3-amino-6-chloro-, dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

L10 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:463090 CAPLUS
DOCUMENT NUMBER: 63:63090
ORIGINAL REFERENCE NO.: 63:11561e-f
TITLE: Pyrazine diuretics. I. N-Amidino-3-amino-6-halopyrazinecarboxamides
AUTHOR(S): Bicking, John B.; Mason, James W.; Woltersdorf, Otto W., Jr.; Jones, James H.; Kwong, Sara F.; Robb, Charles M.; Cragoe, Edward J., Jr.
CORPORATE SOURCE: Merck & Co., Inc., West Point, PA
SOURCE: Journal of Medicinal Chemistry (1965), 8(5), 638-42
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 63:63090
AB A series of N-amidino-3-amino-6-halopyrazinecarboxamides was prepared principally by the reaction of Me 3-amino-6-halopyrazinecarboxylates with guanidine or substituted guanidines. A number of these compds. reverse the electrolyte excretion effects of deoxycorticosterone in the adrenalectomized rat and cause natriuresis in the intact rat and dog while leaving unaffected or even repressing K+ excretion.
IT *96878-31-8*, Pyrazinecarboxamide, N,N'-[ethylenebis[imino(imidocarbonyl)]]bis[3-amino-6-chloro-, hydrochloride (preparation of)
RN 96878-31-8 CAPLUS
CN Pyrazinecarboxamide, N,N'-[ethylenebis[imino(imidocarbonyl)]]bis[3-amino-6-chloro-, hydrochloride (7CI) (CA INDEX NAME)



●x HCl

=> LOG HOLD
COST IN U.S. DOLLARS SINCE FILE TOTAL

∴ NO PRIOR ART.

	ENTRY	SESSION
FULL ESTIMATED COST	56.67	557.70

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.25	-8.25

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:40:33 ON 11 OCT 2006